10/054,967.

cofc

Docket No.: PF115P4C1D1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Letters Patent of:
Kreider et al.

Patent No.: 6,815,420 B2

Issued: November 9, 2004

For: Methods of Using Chemokine Beta-6

REQUEST FOR CERTIFICATE OF CORRECTION PURSUANT TO 37 CFR 1.322

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Upon reviewing the above-identified patent, Patentee noted typographical errors, as well as errors of omission, which should be corrected.

On the Cover Page:

Under "References Cited," insert the following references, which were filed by Applicants and initialed by the Examiner:

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Supplementary European Search Report for Application No. EP 94 91 7388, March 26, 1997.

International Search Report for Application No. PCT/US98/06401, July 31, 1998.--

In the Specification:

At column 36, row 24, delete the header "TABLE 1" and insert -- TABLE 2 -- ;

At columns 37-38, row 1, delete the header "TABLE 2" and insert -- TABLE 3 -- ;

At column 37, row 33, delete the header "TABLE 3" and insert -- TABLE 4 -- .

In the Claims:

In Claim 7, delete "SEQ ID NOs:50, 51, 52, 94, 96, 97 and 99." And insert -- SEQ ID" NOs:50, 51, 53, 94, 96, 97 and 99. --.

In support of the above request, Patentees respectfully note that the references to be cited on the cover page of the issued patent were cited on the Information Disclosure Statement form PTO-1449, submitted July 18, 2002, and in the First Supplemental Information Disclosure Statement form PTO-1449, submitted October 2, 2002, both in connection with the present application. The Examiner-initialed copy of these Information Disclosure Statements are attached hereto as Exhibits A and B, respectively.

Furthermore, Patentees point out the Table 2, 3, and 4 headers were amended as shown above in the Second Preliminary Amendment submitted January 25, 2002 in connection with the present application, a copy of which is attached hereto as Exhibit C.

Finally, Patentees note that claim 7 in the issued should list SEQ ID NO:53 in place of SEQ ID NO:52 as shown above. This is correct because claim 7 in the issued patent corresponds to claim 231 as amended in Applicants response under 37 C.F.R. § 1.111 filed August 22, 2003 which recited "...SEQ ID NOs:50, 51, 53, 94, 96, 97 and 99," a copy of which is attached hereto as Exhibit D.

The above mistakes were not in the application as filed or amended by Patentees, and thus appear to be the fault of the Patent and Trademark Office. Accordingly, it is hereby

requested that a Certificate of Correction under 37 C.F.R. § 1.322 be issued for the above-identified patent. Pursuant to 35 U.S.C. § 254 and 37 C.F.R. § 1.322, no fee is required.

Submitted herewith is a proposed Certificate of Correction (Form PTO/SB/44). Patentees respectfully request the issuance of the Certificate of Correction.

Dated: February 19, 2005

Respectfully submitted,

By _____
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PTO/SB/44 (05-03)
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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,815,420 B2

DATED : November 9, 2004

INVENTOR(S) : Kreider, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Cover Page:

Under "References Cited," insert the following references:

-- U.S. PATENT DOCUMENTS

5,179,078	01/1993	Rollins, et al.
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Villiger, et al., "Monocyte Chemoattractant Protein-1 (MCP-1) Expression in Human Articular Cartilage," *J. Clin. Invest. 90:*488-496 (1992).

Wells, J.A., "Additivity of Mutational Effects in Proteins," *Biochem. 29:*8509-8517 (1990).

Wempe, et al., "Gene Expression and cDNA Cloning Identified a Major Basic Protein Constituent of Bovine Seminal Plasma as Bovine Monocyte-Chemoattractant Protein-1 (MCP-1)," *DNA and Cell Biol. 10:*671-679 (1991).

Yoshimura, et al., "Human Monocyte Chemoattractant Protein-1 (MCP-1): Full-length cDNA Cloning, Expression in Mitogen-stimulated Blood Mononuclear Leukocytes, and Sequence Similarity to Mouse Competence Gene *JE*," *FEBS Letters 244:*487-493 (1989).

Yoshimura, et al., "Molecular Cloning of Rat Monocyte Chemoattractant Protein-1 (MCP-1) and its Expression in Rat Spleen Cells and Tumor Cell Lines," *Biochem. Biophys. Res. Commun. 174:*504-509 (1991).

Yoshimura and Yuhki, "Neutrophil Attractant/Activation Protein-1 and Monocyte Chemoattractant Protein-1 in Rabbit," *J. Immunol. 146:*3483-3488 (1991).

WPI Accession No. 92-185765, English Language Abstract of EP 0 488 900.

Supplementary European Search Report for Application No. EP 94 91 7388, March 26, 1997.

International Search Report for Application No. PCT/US98/06401, July 31, 1998.--

In the Specification:

At column 36, row 24, delete the header "TABLE 1" and insert -- TABLE 2 -- ;

At columns 37-38, row 1, delete the header "TABLE 2" and insert -- TABLE 3 -- ;

At column 37, row 33, delete the header "TABLE 3" and insert -- TABLE 4 -- .

In the Claims:

In Claim 7, delete "SEQ ID NOs:50,51, 52, 94, 96, 97 and 99." And insert -- SEQ ID" NOs:50, 51, 53, 94, 96, 97 and 99. --.

MAILING ADDRESS OF SENDER:
Mark J. Hyman
HUMAN GENOME SCIENCES, INC.
14200 Shady Grove Road
Rockville, Maryland 20850

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO. 1488.034000B/EKS/HCC	APPLICATION NO. 10/054,967
APPLICANT Kreider *et al.*	
FILING DATE January 25, 2002	GROUP 1646

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
EVK	AA1	5,179,078	01/12/1993	Rollins *et al.*	514	2	05/16/1991
	AB1	5,237,051	08/17/1993	Garbers *et al.*	530	350	12/06/1990
	AC1	5,382,658	01/17/1995	Kronis *et al.*	530	397	04/03/1992
	AD1	5,866,373	02/02/1999	Li *et al.*	435	69.5	06/07/1995
	AE1	5,880,263	03/09/1999	Li *et al.*	530	351	10/08/1996
	AF1	6,028,169	02/22/2000	Kreider *et al.*	530	324	12/19/1997
	AG1	6,075,124	06/13/2000	Li *et al.*	530	351	03/20/1998
	AH1	6,100,389	08/08/2000	Li *et al.*	536	23.5	03/20/1998
	AI1	6,379,926 B1	04/30/2002	Kreider *et al.*	435	69.5	10/15/1999
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
EVK	AL1	WO 92/20372 A1	11/26/1992	WIPO			Yes No
	AM1	EP 0 488 900 A1	06/03/1992	Europe			Yes X No
	AN1	WO 95/07985 A1	03/23/1995	WIPO			Yes No
	AO1	WO 95/31467 A1	11/23/1995	WIPO			Yes No
	AP1	WO 96/38559 A1	12/05/1996	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EVK ✓	AR	1	Beall, C.J., *et al.*, "Conversion of Monocyte Chemoattractant Protein-1 into a Neutrophil Attractant by Substitution of Two Amino Acids," *J. Biol. Chem.* *267*:3455-3459, American Society for Biochemistry and Molecular Biology, Inc. (1992).
✓	AS	1	Berkhout, T.A., *et al.*, "Cloning, *in Vitro* Expression, and Functional Characterization of a Novel Human CC Chemokine of the Monocyte Chemotactic Protein (MCP) Family (MCP-4) That Binds and Signals through the CC Chemokine Receptor 2B," *J. Biol. Chem. 272*:16404-16413, American Society for Biochemistry and Molecular Biology (June 1997).
✓	AT	1	Bischoff, S.C., *et al.*, "Monocyte Chemotactic Protein 1 Is a Potent Activator of Human Basophils," *J. Exp. Med. 175*:1271-1275, Rockefeller University Press (1992).

EXAMINER E-Kemmerer — DATE CONSIDERED 5/16/03

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
EEK	AL2	WO 96/40762 A1	12/19/1996	WIPO			Yes No
	AM2	CA 2,152,141	12/20/1996	Canada			Yes No
	AN2	WO 97/15594 A1	05/01/1997	WIPO			Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK ✓	AR	2	Bottazzi, B., *et al.*, "A chemoattractant expressed in human sarcoma cells (tumor-derived chemotactic factor, TDCF) is identical to monocyte chemoattractant protein-1/monocyte chemotactic and activating factor (MCP-1/MCAF)," *Int. J. Cancer* 45:795-797, Wiley-Liss, Inc. (1990).
✓	AS	2	Bowie, J.U., *et al.*, "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," *Science* 247:1306-1310, American Association for the Advancement of Science (1990).
✓	AT	2	Brieland, J.K., *et al.*, "Effect of Acute Inflammatory Lung Injury on the Expression of Monocyte Chemoattractant Protein-1 (MCP-1) in Rat Pulmonary Alveolar Macrophages," *Am. J. Respir. Cell Mol. Biol.* 7:134-139, American Lung Association (1992).

EXAMINER E. Kennemer — DATE CONSIDERED 5/16/03

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK ✓	AR	3	Brieland, J.K., *et al.*, "Expression of Monocyte Chemoattractant Protein-1 (MCP-1) by Rat Alveolar Macrophages during Chronic Lung Injury," *Am. J. Respir. Cell Mol. Biol. 9*:300-305, American Lung Association (1993).
✓	AS	3	Brown, Z., *et al.*, "IL-1 receptor antagonist inhibits monocyte chemotactic peptide-1 generation by human mesangial cells," *Kidney Int. 42*:95-101, Blackwell Scientific Publications (1992).
✓	AT	3	Colditz, I., *et al.*, "*In Vivo* Inflammatory Activity of Neutrophil-Activating Factor, a Novel Chemotactic Peptide Derived from Human Monocytes," *Am. J. Pathol. 134*:755-760, American Association of Pathologists (1989).

EXAMINER E. Kemmeren

DATE CONSIDERED 5/16/03

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK	AR	4	Daniel, C., *et al.*, "Mapping of Linear Antigenic Sites on the S Glycoprotein of a Neurotropic Murine Coronavirus with Synthetic Peptides: A Combination of Nine Prediction Algorithms Fails To Identify Relevant Epitopes and Peptide Immunogenicity Is Drastically Influenced by the Nature of the Protein Carrier," *Virology 202*:540-549, Academic Press, Inc. (1994).
	AS	4	Decock, B., *et al.*, "Identification of the Monocyte Chemotactic Protein from Human Osteosarcoma Cells and Monocytes Detection of a Novel N-Terminally Processed Form," *Biochem. Biophys. Res. Commun. 167*:904-909, Academic Press, Inc. (1990).
	AT	4	Forssmann, U., *et al.*, "Eotaxin-2, a Novel CC Chemokine that Is Selective for the Chemokine Receptor CCR3, and Acts Like Eotaxin on Human Eosinophil and Basophil Leukocytes," *J. Exp. Med. 185*:2171-2176, Rockefeller University Press (June 1997).

EXAMINER E. Flemmeren DATE CONSIDERED 5/16/03

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

✓	AR	5	Furutani, Y., *et al.*, "Cloning and Sequencing of the cDNA for Human Monocyte Chemotactic and Activating Factor (MCAF)," *Biochem. Biophys. Res. Commun.* *159*:249-255, Academic Press, Inc. (1989).
✓	AS	5	Garcia-Zepeda, E.A., *et al.*, "Human Monocyte Chemoattractant Protein (MCP)-4 Is a Novel CC Chemokine with Activities on Monocytes, Eosinophils, and Basophils Induced in Allergic and Nonallergic Inflammation That Signals Through the CC Chemokine Receptors (CCR)-2 and -3," *J. Immunol.* *157*:5613-5626, American Association of Immunologists, Inc. (December 1996).
✓	AT	5	George, D.G., *et al.*, "Current Methods in Sequence Comparison and Analysis," in *Macromolecular Sequencing and Synthesis, Selected Methods and Applications*, Schlesinger, D.H., ed., Alan R. Liss, Inc., New York, New York, pp. 127-149 (1988).

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	AM						Yes No
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EKK ✓	AR	6	Gong, J.-H. and Clark-Lewis, I., "Antagonists of Monocyte Chemoattractant Protein 1 Identified by Modification of Functionally Critical NH_2-terminal Residues," *J. Exp. Med.* *181*:631-640, Rockefeller University Press (1995).
✓	AS	6	Gong, J.-H., *et al.*, "RANTES and MCP-3 Antagonists Bind Multiple Chemokine Receptors," *J. Biol. Chem.* *271*:10521-10527, American Society for Biochemistry and Molecular Biology, Inc. (May 1996).
✓	AT	6	Gronenborn, A.M. and Clore, G.M., "Modeling the three-dimensional structure of the monocyte chemo-attractant and activating protein MCAF/MCP-1 on the basis of the solution structure of interleukin-8," *Protein Eng.* *4*:263-269, Oxford University Press (1991).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK	AR	7	Jose, P.J., *et al.*, "Eotaxin: A Potent Eosinophil Chemoattractant Cytokine Detected in a Guinea Pig Model of Allergic Airways Inflammation," *J. Exp. Med.* *179*:881-887, Rockefeller University Press (1994).
	AS	7	Kao, J., *et al.*, "Endothelial Monocyte-activating Polypeptide II. A Novel Tumor-Derived Polypeptide That Activates Host-Response Mechanisms," *J. Biol. Chem.* *267*:20239-20247, American Society for Biochemistry and Molecular Biology, Inc. (1992).
	AT	7	Kawahara, R.S. and Deuel, T.F., "Platelet-derived Growth Factor-inducible Gene *JE* Is a Member of a Family of Small Inducible Genes Related to Platelet Factor 4," *J. Biol. Chem.* *264*:679-682, American Society for Biochemistry and Molecular Biology, Inc. (1989).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK	AR	8	Koch, A.E., *et al.*, "Enhanced Production of Monocyte Chemoattractant Protein-1 in Rheumatoid Arthritis," *J. Clin. Invest.* 90:772-779, American Society for Clinical Investigation, Inc. (1992).
	AS	8	Kuna, P., *et al.*, "Monocyte Chemotactic and Activating Factor Is a Potent Histamine-releasing Factor for Human Basophils," *J. Exp. Med.* 175:489-493, Rockefeller University Press (1992).
	AT	8	Marston, F.A.O., "The purification of eukaryotic polypeptides synthesized in *Escherichia coli*," *Biochem J.* 240:1-12, Japan Biochemical Society (1986).

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EKK ✓	AR	9	Matsushima, K., *et al.*, "Molecular Cloning of a Human Monocyte-Derived Neutrophil Chemotactic Factor (MDNCF) and the Induction of MDNCF mRNA by Interleukin 1 and Tumor Necrosis Factor," *J. Exp. Med.* *167*:1883-1893, Rockefeller University Press (1988).
✓	AS	9	Matsushima, K., *et al.*, "Purification and Characterization of a Novel Monocyte Chemotactic and Activating Factor Produced by a Human Myelomonocytic Cell Line," *J. Exp. Med.* *169*:1485-1490, Rockefeller University Press (1989).
✓	AT	9	Mehrabian, M., *et al.*, "Localization of Monocyte Chemotactic Protein-1 Gene (SCYA2) to Human Chromosome 17q11.2-q21.1," *Genomics* *9*:200-203, Academic Press, Inc. (1991).

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EEK ✓	AR	10	Minty, A., *et al.*, "Molecular cloning of the MCP-3 chemokine gene and regulation of its expression," *Eur. Cytokine Netw. 4*:99-110, John Libbey Eurotext Ltd. (1993).
✓	AS	10	Morgan, J.G., *et al.*, "Cloning of the cDNA For The Serine Protease Homolog CAP37/Azurocidin, A Microbicidal and Chemotactic Protein from Human Granulocytes," *J. Immunol. 147*:3210-3214, American Association of Immunologists, Inc. (1991).
✓	AT	10	Nelken, N.A., *et al.*, "Monocyte Chemoattractant Protein-1 in Human Atheromatous Plaques," *J. Clin. Invest. 88*:1121-1127, American Society for Clinical Investigation, Inc. (1991).

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✓	AR	11	Ngo, J.T., *et al.*, "Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox," In: *The Protein Folding Problem and Tertiary Structure Prediction*, Merz, Jr., K. and Le Grand, S., eds., Birkhäuser, Boston, Massachusetts, pp. 491-495 (1994).
✓	AS	11	Opdenakker, G., *et al.*, "Human monocyte chemotactic protein-3 (MCP-3): molecular cloning of the cDNA and comparison with other chemokines," *Biochem. Biophys. Res. Comm. 191*:535-542, Academic Press, Inc. (1993).
✓	AT	11	Patel, V.P., *et al.*, "Molecular and Functional Characterization of Two Novel Human C-C Chemokines as Inhibitors of Two Distinct Classes of Myeloid Progenitors," *J. Exp. Med. 185*:1163-1172, Rockefeller University Press (April 1997).

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	AP						Yes No

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EK ✓	AR	12	Pereira, H.A., *et al.*, "CAP37, a Human Neutrophil-derived Chemotactic Factor with Monocyte Specific Activity," *J. Clin. Invest.* *85*:1468-1476, American Society for Clinical Investigation, Inc. (1990).
✓	AS	12	Ransohoff, R.M., *et al.*, "Astrocyte expression of mRNA encoding cytokines IP-10 and JE/MCP-1 in experimental autoimmune encephalomyelitis," *FASEB J.* 7:592-600, Federation of American Societies for Experimental Biology (1993).
✓	AT	12	Robinson, E.A., *et al.*, "Complete amino acid sequence of a human monocyte chemoattractant, a putative mediator of cellular immune reactions," *Proc. Natl. Acad. Sci. USA* *86*:1850-1854, National Academy of Sciences (1989).

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EOK	AR	13	Rolfe, M.W., *et al.*, "Expression and regulation of human pulmonary fibroblast-derived monocyte chemotactic peptide-1," *Am. J. Physiology 263*:L536-L545, American Physiological Society (1992).
✓	AS	13	Rollins, B.J., *et al.*, "Cloning and expression of *JE*, a gene inducible by platelet-derived growth factor and whose product has cytokine-like properties," *Proc. Natl. Acad. Sci. USA 85*:3738-3742, National Academy of Sciences (1988).
✓	AT	13	Rollins, B.J., *et al.*, "The Human Homolog of the *JE* Gene Encodes a Monocyte Secretory Protein," *Mol. Cell. Biol. 9*:4687-4695, American Society for Microbiology (1989).

EXAMINER E. Kemmerer

DATE CONSIDERED 5/16/03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1488.034000B/EKS/HCC	APPLICATION NO. 10/054,967
	APPLICANT Kreider *et al.*	
	FILING DATE January 25, 2002	GROUP 1646

U.S. PATENT DOCUMENTS

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EOT ✓	AR	14	Rudinger, J., "Characteristics of the amino acids as components of a peptide hormone sequence," In: *Peptide Hormones*, Parsons, J.A., ed., University Park Press, Baltimore, Maryland, pp. 1-7 (1976).
✓	AS	14	Russell, M.E., *et al.*, "Early and persistent induction of monocyte chemoattractant protein 1 in rat cardiac allografts," *Proc. Natl. Acad. Sci. USA 90*:6086-6090, National Academy of Sciences (1993).
✓	AT	14	Sacerdote, P., *et al.*, "Cholecystokinin and the Immune System: Receptor-Mediated Chemotaxis of Human and Rat Monocytes," *Peptides 9*:29-34, Pergamon Press (1988).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK ✓	AR	15	Schall, T.J., "Biology Of The RANTES/SIS Cytokine Family," *Cytokine 3*:165-183, W.B. Saunders Co. (1991).
✓	AS	15	Schulz, G.E. and Schirmer, R.H., "Empirical Similarities Between Amino Acid Residues," in *Principles of Protein Structure*, Springer-Verlag, New York, New York, pp. 14-16 (1979).
✓	AT	15	Shyy, Y.-J., *et al.*, "Structure of Human Monocyte Chemotactic Protein Gene and Its Regulation by TPA," *Biochem. Biophys. Res. Commun. 169*:346-351, Academic Press, Inc. (1990).

EXAMINER C. Kemmerer	DATE CONSIDERED 5/16/03

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1488.034000B/EKS/HCC	APPLICATION NO. 10/054,967
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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EJK	AR	16	Strieter, R.M., *et al.*, "Disparate Gene Expression of Chemotactic Cytokines by Human Mononuclear Phagocytes," *Biochem. Biophys. Res. Commun. 166*:886-891, Academic Press, Inc. (1990).
✓	AS	16	Uguccioni, M., *et al.*, "Monocyte Chemotactic Protein 4 (MCP-4), a Novel Structural and Functional Analogue of MCP-3 and Eotaxin," *J. Exp. Med. 183*:2379-2384, Rockefeller University Press (May 1996).
✓	AT	16	Van Damme, J., *et al.*, "Production and identification of natural monocyte chemotactic protein from virally infected murine fibroblasts: Relationship with the product of the mouse competence (JE) gene," *Eur. J. Biochem. 199*:223-229, Blackwell Science Ltd. (1991).

EXAMINER E. Kemmerer — DATE CONSIDERED 5/16/03

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FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.	APPLICATION NO.
1488.034000B/EKS/HCC	10/054,967
APPLICANT: Kreider *et al.*	
FILING DATE: January 25, 2002	GROUP: 1646

U.S. PATENT DOCUMENTS

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK ✓	AR	17	Van Damme, J., *et al.*, "Structural and Functional Identification of Two Human, Tumor-derived Monocyte Chemotactic Proteins (MCP-2 and MCP-3) Belonging to the Chemokine Family," *J. Exp. Med. 176*:59-65, Rockefeller University Press (1992).
✓	AS	17	Villiger, P.M., *et al.*, "Monocyte Chemoattractant Protein-1 (MCP-1) Expression in Human Articular Cartilage," *J. Clin. Invest. 90*:488-496, American Society for Clinical Investigations, Inc. (1992).
✓	AT	17	Wells, J.A., "Additivity of Mutational Effects in Proteins," *Biochem. 29*:8509-8517, American Chemical Society (1990).

EXAMINER E. Kemmerer

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EWK	AR	18	Wempe, F., *et al.*, "Gene Expression and cDNA Cloning Identified a Major Basic Protein Constituent of Bovine Seminal Plasma as Bovine Monocyte-Chemoattractant Protein-1 (MCP-1)," *DNA and Cell Biol. 10*:671-679, Mary Ann Liebert, Inc. (1991).
	AS	18	Yoshimura, T., *et al.*, "Human monocyte chemoattractant protein-1 (MCP-1): Full-length cDNA cloning, expression in mitogen-stimulated blood mononuclear leukocytes, and sequence similarity to mouse competence gene JE," *FEBS Letters 244*:487-493, Elsevier Science B.V. (1989).
	AT	18	Yoshimura, T., *et al.*, "Molecular Cloning of Rat Monocyte Chemoattractant Protein-1 (MCP-1) and Its Expression In Rat Spleen Cells and Tumor Cell Lines," *Biochem. Biophys. Res. Commun. 174*:504-509, Academic Press, Inc. (1991).

EXAMINER E. Kemmerer	DATE CONSIDERED 5/16/03

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FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1488.034000B/EKS/HCC	APPLICATION NO. 10/054,967
	APPLICANT Kreider *et al.*	
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK	AR	19	Yoshimura, T. and Yuhki, N., "Neutrophil Attractant/Activation Protein-1 And Monocyte Chemoattractant Protein-1 In Rabbit," *J. Immunol.* *146*:3483-3488, American Association of Immunologists, Inc. (1991).
	AS	19	~~WPI Accession No. 92-185765, English Language Abstract of EP 0 488 900 (Document AM1).~~ CONSIDERED; DO NOT PRINT
	AT	19	~~Supplementary European Search Report for Application No. EP 94 91 7388, completed~~ March 26, 1997. CONSIDERED; DO NOT PRINT

EXAMINER C. Kemmerer — DATE CONSIDERED 5/16/03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449 INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1488.034000B/EKS/HCC	APPLICATION NO. 10/054,967
	APPLICANT Kreider *et al.*	
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EEK	AR	20	~~International Search Report for Application No. PCT/US98/06401, mailed July 31, 1998.~~ CONSIDERED; ~~DO NOT PRINT~~
↓	AS	20	~~Pending Non Provisional U.S. Patent Application No. 09/912,293, Rosen et al., filed July 26, 2001, pp. 1-75 (pages 1 & 2 partially redacted); portion of~~ Table 2; and ~~SEQ ID NO:126873, UNPUBLISHED.~~ ~~CONSIDERED; DO NOT PRINT~~
	AT		

EXAMINER E. Kimmel	DATE CONSIDERED 5/16/03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.	APPLICATION NO.
1488.034000B/EKS/HCC/VSR	10/054,967
APPLICANT: KREIDER *et al.*	
FILING DATE: January 25, 2002	GROUP: 1646

U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
EKK	AO2	WO 98/44118 A1	10/08/1998	WIPO			Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR		
	AS		
EKK ✓	AT	20	Broxmeyer, H.E., *et al.*, "Effects of CC, CXC, C, and CX3C Chemokines on Proliferation of Myeloid Progenitor Cells, and Insights into SDF-1-Induced Chemotaxis of Progenitors," *Ann. N.Y. Acad. Sci. 872*:142-163, New York Academy of Sciences (April 1999)

EXAMINER: E. Kemmerer — DATE CONSIDERED: 5/16/03

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

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FORM PTO-1449 FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 1488.034000B/EKS/HCC/VSR	APPLICATION NO. 10/054,967
	APPLICANT KREIDER *et al.*	
	FILING DATE January 25, 2002	GROUP 1646

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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EOK ✓	AR	21	Salcedo, T.W., *et al.*, "Structure-Function Analysis of Eotaxin-2/CKβ-6/MPIF-2," *FASEB J. 13*:A317, Abstract No. 252.17, Federation of American Societies for Experimental Biology (March 1999)
	AS		
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EXAMINER E. Kennrem

DATE CONSIDERED 5/16/03

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: KREIDER *et al.* Appl. No. *To be assigned* (Divisional of U.S. Appl. No. 09/419,281; Filed: October 15, 1999) Filed: *Herewith* For: **Methods of Using Chemokine β-6 (as amended herein)**	Art Unit: *To be assigned* Examiner: *To be assigned* Atty. Docket: 1488.034000B/EKS/HCC

Second Preliminary Amendment

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, please amend the application as follows. This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.115; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

Please amend the application as follows:

In the Specification:

Please replace the paragraph beginning at page 12, line 3, with the following paragraph:

FIG. 11A and 11B illustrate the effect of Ckβ-6 on histamine and LTC4 release from human eosinophils and the ability of anti-CCR3 to block such activity.

Please replace the paragraph beginning at page 14, line 16, with the following paragraph:

In accordance with an aspect of the present invention, there is provided an isolated nucleic acid (polynucleotide) which encodes for the full-length or mature polypeptide having the deduced amino acid sequence of Figure 1 (SEQ ID NO:2) or for the mature polypeptide encoded by the cDNA of the clone deposited at the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209, as ATCC Deposit No. 75703 on March 10, 1994.

Please replace the text at page 61, line 11, with the following text:

Table 2

Please replace the text at page 62, line 8, with the following text:

Table 3

Please replace the text at page 63, line 3, with the following text:

Table 4

Please replace the paragraph beginning at page 101, line 24, with the following paragraph:

The effect of Ckβ-6 on the distribution of the primitive hematopoietic progenitors in peripheral blood, spleen, and bone marrow was studied in 16 week old C57B1/6 mice (about 20 g).

In the first experiment, 3 mice were injected i.p. daily with 1 mg/kg Ckβ-6 or saline for 2 days and analyzed 24 hours after the last injection. In the second experiment, another 3 mice were injected i.p. daily with 1 mg/kg Ckβ-6 or saline for 4 days and analyzed 24 hours after the last injection. In both the experiments, the blood of each animal was collected by cardiac puncture and the mice were sacrificed to obtain bone marrow and spleens. The indicated number of cells from each of the tissues was then plated in duplicates in agar-containing medium in the presence of 5 ng/ml IL-3, 50 ng/ml SCF, 5 ng/ml M-CSF and 10 ng/ml IL-1a and incubated for 14 days. In the 2 experiments, the data from the different animals were pooled and expressed as mean ± S.D. The results of both experiments shows that Ckβ-6 mobilize stem cells from bone marrow to peripheral blood (Tables 2 and 3). In the first experiment, after 2 days of treatment with Ckβ-6, the frequency of HPP-CFC, LPP-CFC and immature cells in peripheral blood increased significantly over the controls. No changes were observed in the spleen and a significant decrement of HPP-CFC was observed in the bone marrow (Table 2). In the second experiment, after 4 days of treatment with Ckβ-6, the same significant increment of HPP-CFC, LPP-CFC and immature cells frequency was observed in peripheral blood. A significant increment of immature cells frequency was observed in the spleen and a significant decrement of HPP-CFC and LPP-CFC was observed in the bone marrow Table 3. In particular it is important to note the presence of immature hematopoietic cells in the peripheral blood after the injection of Ckβ-6. The effect was observed in the animals treated with Ckβ-6 was not due to toxicity as the FACScan profile of the leukocyte composition of both the control and the mice treated with Ckβ-6 is identical Table 4.

Remarks

The specification has been amended to update the address of the ATCC and to correct typographical errors. No new matter has been added by these amendments.

Conclusion

Applicants believe that this application is in condition for substantive examination. Early notice to this effect is respectfully requested. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Helene C. Carlson
Agent for Applicants
Registration No. 47,473

Date: Jan. 25, 2002

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Versions with Markings to show changes made

In the Specification:

The paragraph beginning at page 12, line 3:

FIG. 11A and 11B illustrate[s] the effect of Ckβ-6 on histamine and LTC4 release from human eosinophils and the ability of anti-CCR3 to block such activity.

The paragraph beginning at page 14, line 16:

In accordance with an aspect of the present invention, there is provided an isolated nucleic acid (polynucleotide) which encodes for the full-length or mature polypeptide having the deduced amino acid sequence of Figure 1 (SEQ ID NO:2) or for the mature polypeptide encoded by the cDNA of the clone deposited at the American Type Culture Collection, [12301 Parklawn Drive, Rockville, Maryland 20852]10801 University Boulevard, Manassas, Virginia 20110-2209, as ATCC Deposit No. 75703 on March 10, 1994.

The text at page 61, line 11:

[Table 1]Table 2

The text at page 62, line 8:

[Table 2]Table 3

The text at page 63, line 3:

[Table 3]Table 4

The paragraph beginning at page 101, line 24:

The effect of Ckβ-6 on the distribution of the primitive hematopoietic progenitors in peripheral blood, spleen, and bone marrow was studied in 16 week old C57B1/6 mice (about 20 g). In the first experiment, 3 mice were injected i.p. daily with 1 mg/kg Ckβ-6 or saline for 2 days and analyzed 24 hours after the last injection. In the second experiment, another 3 mice were injected i.p. daily with 1 mg/kg Ckβ-6 or saline for 4 days and analyzed 24 hours after the last injection. In both the experiments, the blood of each animal was collected by cardiac puncture and the mice were sacrificed to obtain bone marrow and spleens. The indicated number of cells from each of the tissues was then plated in duplicates in agar-containing medium in the presence of 5 ng/ml IL-3, 50 ng/ml SCF, 5 ng/ml M-CSF and 10 ng/ml IL-1a and incubated for 14 days. In the 2 experiments, the data from the different animals were pooled and expressed as mean ± S.D. The results of both experiments shows that Ckβ-6 mobilize stem cells from bone marrow to peripheral blood [[Tables 1 and 2]](Tables 2 and 3). In the first experiment, after 2 days of treatment with Ckβ-6, the frequency of HPP-CFC, LPP-CFC and immature cells in peripheral blood increased significantly over the controls. No changes were observed in the spleen and a significant decrement of HPP-CFC was observed in the bone marrow [[Table 1]](Table 2). In the second experiment, after 4 days of treatment with Ckβ-6, the same significant increment of HPP-CFC, LPP-CFC and immature cells frequency was observed in peripheral blood. A significant increment of immature cells frequency was observed in the spleen and a significant decrement of HPP-CFC and LPP-CFC was observed in the bone marrow [[Table 2]]Table 3. In particular it is important to note the presence of immature hematopoietic cells in the peripheral blood after the injection of Ckβ-6. The effect was observed in the animals treated with Ckβ-6 was not due to toxicity as the FACScan profile of the leukocyte composition of both the control and the mice treated with Ckβ-6 is identical [[Table 3]]Table 4.

RETURN RECEIPT CARD
(MPEP § 503)

OIPE:	Please Date Stamp In The Box Below And Return To Addressee

Application of:
Kreider et al.

Docket No.: PF115P4C1D1

Application Serial No.: 10/054,967-Conf. #9197

Art Unit: 1646

Filed: January 25, 2002

Examiner: E. Kemmerer

Title: Methods of Using Chemokine Beta-6

The following documents were filed by Human Genome Sciences, Inc. via hand delivery on August 22, 2003:

1. Fee Transmittal (1 page)
2. Amendment and Response Under 37 C.F.R. § 1.111

Sender's Initials: MMW/MJH/vr

MAR 4 2005

VIA HAND DELIVERY AUGUST 22, 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Kreider et al.

Atty. Docket No.: PF115P4C1D1

Application No.: 10/054,967

Group Art Unit: 1646

Filed: January 25, 2002

Examiner: E. Kemmerer

For: Methods of Using Chemokine Beta-6

AMENDMENT AND RESPONSE UNDER 37 C.F.R. § 1.111

Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed May 22, 2003 (Paper No. 10), please consider the following amendments and remarks. Applicants submit a Fee Transmittal Sheet concurrently herewith.

Please amend the application as follows:

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims.

Listing of Claims:

1-40 (Canceled)

41. (Currently amended) A method of inhibiting the activation or mobilization of eosinophils in an individual in need thereof comprising administering to said individual a therapeutically effective amount of a polypeptide consisting of ~~an amino acid sequence shown in any one of SEQ ID NOs:23-114~~ the amino acid sequence of SEQ ID NO:48.

42. (Previously presented) The method of claim 41, wherein said polypeptide is fused to polyethylene glycol.

43. (Previously presented) The method of claim 41, wherein said polypeptide is fused to a heterologous polypeptide.

44-135 (Canceled)

136. (Currently amended) A method of inhibiting the activation or mobilization of basophils in an individual in need thereof comprising administering to said individual a therapeutically effective amount of a polypeptide consisting of ~~an amino acid sequence shown in any one of SEQ ID NOs:23-114~~ the amino acid sequence of SEQ ID NO:48.

137. (Previously presented) The method of claim 136, wherein said polypeptide is fused to polyethylene glycol.

138. (Previously presented) The method of claim 136, wherein said polypeptide is fused to a heterologous polypeptide.

139-230 (Canceled)

231. (New) A method of inhibiting the activation or mobilization of eosinophils in an individual in need thereof comprising administering to said individual a therapeutically effective amount of a polypeptide consisting of an amino acid sequence shown in any one of SEQ ID NOs:50, 51, 53, 94, 96, 97, and 99.

232. (New) The method of claim 231, wherein said polypeptide is fused to polyethylene glycol.

233. (New) The method of claim 231, wherein said polypeptide is fused to a heterologous polypeptide.

234. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:50.

235. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:51.

236. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:53.

237. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:94.

238. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:96.

239. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:97.

240. (New) The method of claim 231, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:99.

241. (New) A method of inhibiting the activation or mobilization of basophils in an individual in need thereof comprising administering to said individual a therapeutically effective amount of a polypeptide consisting of an amino acid sequence shown in any one of SEQ ID NOs:50, 51, 53, 94, 96, 97, and 99.

242. (New) The method of claim 241, wherein said polypeptide is fused to polyethylene glycol.

243. (New) The method of claim 241, wherein said polypeptide is fused to a heterologous polypeptide.

244. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:50.

245. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:51.

246. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:53.

247. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:94.

248. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:96.

249. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:97.

250. (New) The method of claim 241, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:99.

Remarks

Claims 44-135 and 139-230 have been canceled without prejudice or disclaimer, and claims 41 and 136 have been amended to recite only SEQ ID NO:48. Further, claims 231 to 250 have been added. Claims 231-250 correspond to claims 71-72, 74, 115, 117-118, 120, 166-167, 169, 210, 212-213, and 215, and in part to dependent claims 42-43 and 137-138. These amendments are fully supported by the specification as filed as detailed below, and thus no new matter has been added.

Claims 41-43, 136-138, and 231-250 are pending. The Examiner has indicated that claim 69 would be allowable if rewritten in independent form. Applicants note that independent claim 41, from which claim 69 depended, has been amended to refer only to the subject matter of claim 69. Further, the Examiner made no specific rejection to dependent claims 42-43. Accordingly, Applicants respectfully submit that claims 41-43 are in condition for allowance.

Applicants thank the Examiner for the reconsideration and withdrawal of the previous restriction requirement.

I. Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

The Examiner has rejected claims 136-230 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *See* Paper No. 10, page 3. In particular, the Examiner contends that "[t]he specification as originally filed does not disclose the concept of inhibiting the activation or mobilization of basophils using the peptides recited in the claims. The concept is not specifically disclosed, and does not flow naturally from the specification." *Id.*

In response, Applicants respectfully disagree and traverse. Preliminarily, Applicants apologize for the failure to more clearly identify the support for claims 136-230 in the preliminary amendment; such support is identified below. Applicants also note that claims 139-230 have been canceled without prejudice or disclaimer, thereby mooting any rejection of such claims. However, Applicants respond to the instant rejection as it may be applied to pending claims 136-138 and 241-250.

Original claim 18 specifically recites a method "wherein said polypeptide inhibits activation or moblization [sic] of basophils." The antecedent polypeptide for claim 18 includes the polypeptides recited in the claims, such as Pro (4) to Arg (73) of SEQ ID NO:2, *i.e.*, SEQ ID NO:48. *See* original claims 1 and 6. Thus, the specification specifically claims the concept of inhibiting the activation or mobilization of basophils using the peptides recited in the present claims.

Moreover, the specification teaches that CkB-6 acts as a chemoattractant for both eosinophils and basophils. *See* pages 11-12 (description of Figures 10-12), and 106-107 (Examples 10-11). The specification also teaches that negative dominant mutants of Ckβ-6, such as the polypeptide antagonists recited in the claims, bind to the Ckβ-6 receptor (CCR3), but fail to activate the cells to which they bind. *See* page 41, lines 5-29, and page 65, line 24 to page 66, line 6. The specification further teaches that basophils express CCR3. *See, e.g.*, page 107 (Example 11). Based on the above, the specification discloses methods for using such antagonists inhibit the activation or mobilization of basophils, including:

> The antagonists may be employed to treat inflammation by preventing the attraction of eosinophils or basophiles [sic] to a wound or a site of trauma, and to regulate normal pulmonary macrophage populations, since acute and chronic inflammatory pulmonary diseases are associated with sequestration of mononuclear phagocytes in the lung. They may also be employed to treat rheumatoid arthritis, since MCP levels were found to be significantly elevated in synovial fluid from rheumatoid arthritis patients which suggests that synovial production of Ckβ-6 attracts eosinophils or basophils whose influx and activation are important in the pathogenesis of both degenerative and inflammatory arthropathies.
>
> The antagonists may also be employed to prevent allergies, since it has been shown that MCPs directly induce histamine release by basophils. Related immunological disorders including late phase allergic reactions, chronic urticaria, and atopic dermatitis can be treated by antagonists which are effective to inhibit chemokine-induced mast cell and basophil degranulation and release of histamine. ...
>
> Antagonists may also be employed to treat rheumatoid arthritis by preventing the attraction of eosinophils and basophils into synovial fluid in the joints of patients.
>
> Page 67, line 13 to page 68, line 9.

Thus, the specification specifically discloses and claims the concept of inhibiting the activation or mobilization of basophils using the peptides recited in the present claims. Applicants respectfully assert that one skilled in the art would reasonably conclude that the inventors had possession of the claimed methods of inhibiting both eosinophils and basophils upon reading the specification as filed. Therefore, the instant rejection under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description should be reconsidered and withdrawn.

II. Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

The Examiner has rejected claims 41-68 and 70-135 under 35 U.S.C. § 112, first paragraph, as allegedly not enabling a person skilled in the art to make and use the invention commensurate in scope with the claims. *See* Paper No. 10, pages 3-5. In particular, the Examiner accepts that the specification is enabling for the claimed invention wherein a polypeptide consisting of SEQ ID NO:48 is administered, but contends that it "does not reasonably provide enablement for administration of any other polypeptides to inhibit the activation or mobilization of eosinophils;" Applicants presume that the Examiner also intended the assertion to apply to the activation or mobilization of basophils. Specifically, the Examiner notes that the specification teaches that SEQ ID NO:48 (residues 4-73 of SEQ ID NO:2) inhibited chemotaxis of eosinophils *in vitro*, but contends that the specification provides "no guidance regarding what sequences other than those three amino acid residues can be deleted without loss or change of activity."

In response, Applicants respectfully disagree, and assert that the previously pending claims are fully enabled by the specification in accordance with 35 U.S.C. § 112, first paragraph. However, Applicants note that claims 44-135 and 139-230 have been canceled without prejudice or disclaimer, rendering any rejection of those claims moot. Further, claims 41 and 136 have been amended to recite only SEQ ID NO:48 (which the Examiner has agreed is enabled), thus obviating the rejection as to claims 41-43 and 136-138. Applicants respond to the instant rejection as it may be applied to new claims 231-250, which recite SEQ ID NOS:50, 51, 53, 94, 96, 97, and 99.

The test for enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information

known in the art without undue experimentation. *See, e.g.*, M.P.E.P. § 2164.01(a). In the instant case, Applicants note that the Examiner has not addressed page 41, lines 5-15 of the specification, which teaches that:

> The present invention further relates to Ckβ-6 antagonists. In particular, a deletion of the first three N-terminal amino acid residues of the mature Ckβ-6 protein (i.e., a deletion of Val(1) to Ile(3) in SEQ ID NO:2) results in a polypeptide having antagonistic activity. Thus, according to the present invention, Ckβ-6 antagonists are provided wherein the amino terminus is residue 4 of SEQ ID NO:2 and the carboxyl terminus is residue m, wherein m is any residue of SEQ ID NO:2 from residue 48 to residue 93. Specific Ckβ-6 antagonists according to the present invention include, but are not limited to: Pro(4) to Arg(73); Pro(4) to Arg(75); Pro(4) to Ala(76); Pro(4) to Ala(78). Optionally, the Ckβ-6 antagonists of the present invention can include a Met residue at the N-terminus.

Thus, Applicants respectfully disagree with the Examiner, and note that specific guidance is given as to which polypeptides sequences act as antagonists capable of inhibiting eosinophil or basophil activation or mobilization. Moreover, the specification teaches several assays for verifying that a particular Ckβ-6 antagonist as described above inhibits eosinophil or basophil activation or mobilization, including an *in vitro* chemotaxis assay as described in Example 10, an *in vitro* calcium (Ca2+) release assay as described in Example 9, and an *in vivo* assay as described in Example 12. *See* pages 105-108. The use of such assays would be routine by one skilled in the art. While the Examiner has specifically noted the results of these assays as regarding SEQ ID NO:48, only a cursory assertion has been made as to why it would constitute undue experimentation for one skilled in the art to verify the remaining antagonists using the disclosed assays.

Applicants also point out that 35 U.S.C. § 112, first paragraph, only requires that Applicants enable what is claimed. As noted above, the scope of the pending claims is not identical to the previously pending claims. In particular, Applicants point out that claims 231-250 are directed to SEQ ID NOS: 50, 51, and 53, corresponding to the specific Ckβ-6 antagonists described above other than SEQ ID NO:48, and to SEQ ID NOS:94, 96, 97, and 99, which correspond to SEQ ID NOS:48, 50, 51, and 53 with the addition of a Met residue at the N-terminus. In light of the guidance given in the specification that "a deletion of Val(1) to Ile(3) in SEQ ID NO:2 results in a polypeptide having antagonistic

activity," and the specific description of SEQ ID NOS: 48, 50, 51, 53, 94, 96, 97, and 99 as antagonists at page 41, lines 5-15, the pending claims are fully enabled.

Accordingly, Applicants assert that the pending claims are in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection be reconsidered and withdrawn.

Conclusion

Entry of the above remarks is respectfully solicited. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Respectfully submitted,

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